A review: E.coli Resistance towards Beta-lactam Antibiotics

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Abstract:
Background: Escherichia coli is a gram-negative, coccobacillus, and facultative anaerobes bacterium. E.coli is the main pathogenic bacteria that cause infection in outpatient and inpatient. E. coli causes 85% of UTIs (Urinary Tract Infections) and about 50% of nosocomial infections. E.coli also causes other infections such as diarrhea, sepsis, and meningitis. Antibiotics resistance has become a global health issue. It causes 150 000 death worldwide. The aim of this literature review is to study the scientific literature related to research on E.coli resistance towards beta-lactam antibiotics from clinical samples in various hospitals in 2010-2020.
Method: The method of this review was by collecting various primary literatures such as international journals published in the last 10 years (2010-2020) from the official websites.
Result: Antibiotics resistance of ten beta-lactam antibiotics tested was obtained. The percentage of antibiotics resistance in each antibiotics were as follow : penicillin 100 %; ampicillin 72,82%; amoxicillin 90,86 %; cefotaxime 83,8 % ; cefuroxime 79,56 % ; cefixime 80,87 %; cefazolin 92,43 %; ceftazidime 76,96 %; ceftriaxone 71,90 %; and Imipenem 22,78 %.
Conclusion: The highest level of resistance was penicillin with 100 % and the lowest was Imipenem at 22,78 %.
Key words: Escherichia coli, resistance, beta-lactam antibiotics

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I. Introduction

Escherichia coli is a gram-negative, coccobacillus, facultative anaerobes bacteria that has 0,4-0,7 μm x 1,4 | μm sized flagel and comes from the Enterobacteriaceae family (1). E.coli normally live in a healthy human and animal intestinal tract. E.coli becomes pathogenic when the number of bacteria inside or outside the intestine increases as they release the enterotoxin that can cause infections (2).

E.coli is the main pathogenic bacteria that cause infection in outpatient and inpatient. E. coli causes 85% of UTIs (Urinary Tract Infections) and about 50% of nosocomial infections (3). E.coli also causes other infections such as diarrhea, sepsis, and meningitis (2). In 2015, based on the resistance and bacterial mapping in hospitals such as dari RSUP Cipto Mangunkusumo Jakarta, RSUP Hasan Sadikin Bandung, RSUD Dr. Soetomo Surabaya, RSUD Dr. Saiful Anwar Malang and RSUP Sanglah Denpasar, it was found that infection caused by E.coli was the most prevalent (32.1%), followed by Pseudomonas aeruginosa (17 %), and Klebsiella pneumoniae (14,5 %).

Infection caused by E.coli is treated with antibiotics such as ampicillin, cotrimoxazole, chloramphenicol, tetracyclines, cephalosporins, mezlocillin, and quinolones. The most commonly used is the beta-lactam antibiotics. Beta-lactam antibiotics act by inhibiting the protein synthesis of the bacterial cell wall. This antibiotics target the Penicillin-binding protein (PBP) (5).

Antibiotics resistance has become a global health issue. It causes 150000 death worldwide. Approximately 25 000 people in Europe died from infection caused by multidrug-resistant bacteria and 2 million people in the United States were infected by bacteria each year (6).

II. Material and Method

The literature study was carried out by collecting literatures on E.coli resistance towards beta-lactam antibiotics from the web of science database, pubmed, google scholar, science direct, and research gate. The key words used were "Escherichia coli" dan "Beta lactam antibiotics resistance"

III. Result
Table 1. E.coli resistance pattern towards beta-lactam antibiotics

Antibiotics	Sampling Location	Sample	Number of isolates	Resistant isolates	% Resistance	Reference
Penicillin	UTI and avian colibacillosis patients	Urine	50	50	100%	(7)
	UTI patient from Punjab Hospital, Iran	Urine, earwax, wound swab, eye discharge	321	321	100%	(8)
	UTI patient from Abobo-Avocatier Hospital, North of Abidjan (Côte d'Ivoire)	Urine	14	14	100%	(9)
Ampicillin	UTI patient from Secondary Care Hospital, Medan	Urine	10	8	80%	(10)
	Diarrhea patient from Dr. M. Djamil Hospital, Padang	Feces	92	60	65,3%	(11)
	UTI patient from Dr. Soetomo General Hospital	Urine	41	30	73,17%	(12)
Amoxicillin	Clinical sample from Dessie regional Laboratory Ethiophia	Urine	121	104	86%	(13)
	UTI and avian colibacillosis patients	Urin	50	43	86%	(7)
	UTI patient from Punjab Hospital, Iran	Urine	321	321	100%	(8)
Cefotaxime	Cancer patient from an Hospital in Sudan	Urine, pus, blood, and sputum	54	54	100%	(14)
	UTI patient from Secondary Care Hospital, Medan	Urine	10	6	60%	(10)
	UTI patient from Sanandaj	Urine	151	78	51,89%	(15)
Cefuroxime	Inpatient at Imam Reza Hospital, Tabriz, Iran	Urine	46	42	91,66%	(16)
	UTI patient from Punjab Hospital, Iran	Urine	321	187	58,2%	(8)
	UTI patient from Gadhinagar Hospital, India	Urine	66	59	90 %	(17)
Cefixime	UTI patient from Sanandaj	Urine	273	256	93,81%	(15)
	UTI and avian colibacillosis patients	Urine	50	27	54%	(7)
	Inpatient at Imam Reza Hospital, Tabriz, Iran	Urine	46	31	66,66%	(16)
Cefazolin	UTI patient in Iraq	Urine	74	67	91,3%	(18)
	UTI patient from Dr. Soetomo General Hospital	Urine	41	33	80,49%	(12)
	Inpatient at children's ward of Prof. Dr. R.D. Kandou Hospital, Manado	Feces	30	30	100%	(19)
Ceftazidime	UTI patient from Punjab Hospital, Iran	Urine	237	175	73,8%	(8)
	UTI patient from Dr. Soetomo General Hospital, Surabaya	Urine	127	96	75,6%	(20)
	Cancer patient from an Hospital in Sudan	Urine, pus, blood, and sputum	54	44	81,5%	(14)
Ceftriaxone	UTI patient from Karnataca Hospital	Urine	395	262	66,58%	(21)
	Cancer patient from an Hospital in Sudan	Urine, pus, blood, and sputum	54	50	92,6%	(14)
	UTI patient at Tabriz City	Urine	2850	1611	56,53%	(22)
Imipenem	UTI patient from Dr. Soetomo General Hospital,	Urine	41	6	14,63 %	(12)
	UTI patient from Punjab Hospital, Iran	Urine	321	139	43,3 %	(8)
	Inpatient at Imam Reza Hospital, Tabriz, Iran	Urine	46	5	10,41 %	(16)

IV. Discussion

Resistance pattern and antibiotic sensitivity are important in determining the correct therapy to treat infection especially infection caused by bacteria. Bacterial resistance is one of the complicating factors in infection treatment (4). Bacterial resistance against antibiotic has become the global concern. One of the antibiotic resistant bacteria is the *E.coli* which is mainly resistant towards the beta-lactam antibiotics. *E.coli* is a gram-negative bacteria that comes from the *Enterobacteriaceae* family and a part of the normal bacterial flora but will become pathogenic when their number increases. *E.coli* usually invades the digestive and excretion system. Antibiotic sensitivity test toward *E.coli* isolate can be carried out using the Kirby Bauer methods or measuring the zone of inhibition and interpreting the result with the and Laboratory Standards Institute (CLSI).

Antibiotics resistance test in ten beta-lactam antibiotics were obtained. The percentage of antibiotics resistance in each antibiotics were as follow : penicillin 100 %; ampicillin 72,82%; amoxicillin 90,86 %; cefotaxime 83,8 % ; cefuroxime 79,56 % ; cefixime 80,87 %; cefazolin 92,43 %; ceftazidime 76,96 %; ceftriaxone 71,90 %; and Imipenem 22,78 %. Antibiotics that show the highest resistance were penicillin with the higest percentage of resistance of 100% while the lowest was Imipenem with 22,78 %.

Bacterial resistance against beta-lactam antibiotics occur based on one or more of the following mechanisms : Reduced accumulation of antibiotic in gram-negative bacteria through changes in porins (reduce the access of water soluble β-lactam) or over-expression of efflux pumps (mainly effect the lipophilic β-lactam). Production of hydrolytic enzyme, β-lactamase, coded by gene carried by chromosome or plasmid. β-lactamase contain serine or zinc (Zn^{2+}) protease that has high affinity towards β-lactam hence cutting the amide bond. β-lactamase mainly opens the β-lactam ring with the same mechanism as transpeptidase namely with hydrolyzing the β-lactam ring to inactivate the antibiotic. The third mechanism is through modification of PBP, mainly PBP2 that plays an important role in the formation of bacteria (23).

β-lactam antibiotics were commonly used worldwide. β-lactam antibiotics act by inhibiting the protein synthesis of the bacterial cell wall. β-lactam targets the Penicillin-binding protein (PBP). As the drug attached to the receptor, the action of transpeptidase will be inhibited hence inhibiting the synthesis of peptidoglycan. The antibiotics will become inactive and autolytic enzyme inhibitor on the cell wall will be loss. Activation of autolytic enzymes will cause bacterial lysis (5). The widespread use and abuse of β-lactam antibiotics has provoked β-lactam resistance for decades (24).

V. Conclusion

It can be concuded that antibiotics with the highest level of resistance (100%) toward *E.coli* isolates were Cefotaxime, Cefuroxime, Penicillin, Cefazolin, and Amoxicillin while the lowest (56.3%) was Ceftriaxone.

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